

REMARKS

Applicants have amended claim 21 to insert the limitations of claim 24 which requires that one of β^1 and β^2 confers agonist activity and the other confers antagonist activity. Applicants recognize that claim 24 was withdrawn from consideration as directed to a non-elected invention; however, the Office kindly concludes on page 5 of the Office action that claim 27 would be allowable because “there is no motivation in the prior art to combine agonist activity with antagonist activity in the same complex.” Thus, it is assumed that the Office has already taken this possibility into consideration and that inclusion of this limitation would not impose further burden of search and examination.

In view of inserting this phrase, the proviso formerly in claim 21 becomes unnecessary. In claims 25, 26 and 27, those limitations that do not conform to the added limitation to claim 21 have been deleted and claim 24 has, of course, been canceled. Claim 28 has been amended to indicate that the pharmaceutical formulation consists essentially of an efficient amount of the composition of claim 21 to eliminate the possibility that uncomplexed single-chain forms might be present. This clearly distinguishes the compositions from the supernatants in the Hyde abstract where the authors conclude that the activity of the β subunit associated with the single-chain form might be conferred by the single-chain form alone, and not by the complex. This amendment may be superfluous in view of the amendment to claim 21, but applicants propose it for clarity and ease of prosecution.

Turning, now, to the text of the Office action, applicants greatly appreciate the withdrawal of certain rejections previously made. In view of the denial of priority to the ‘501 patent, a disclaimer of this priority is enclosed. The matters of terminal disclaimer and specification are formal and need not be commented upon.

The outstanding rejection under 35 U.S.C. § 103 of claims 21-23, 25 and 28 over the combination of De Rosa, *et al.*, with Hyde is now obviated as kindly acknowledged by the Examiner by virtue of the limitation now inserted into claim 21.

Therefore, it is believed there are no obstacles to the patentability of the pending claims 21-23 and 25-28 and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 295002005901.

Respectfully submitted,

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